REMARKS

Claims 1-10, 12, 13 and 16-25 are pending in this application. Claims 4-7, 9 and 16-22 have been withdrawn as being directed to non-elected inventions. The issues are addressed below in the order in which they were raised in the Office Action.

Rejection under 35 U.S.C. § 112, First Paragraph

The Action states that claims 1-3, 8, 10, 12, 13 and 23-25 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description in the specification. Specifically, the Action states that the specification does not provide the complete structure of a peptide comprising an AcetylCoA carboxylase (ACCase) having a deleted biotin binding (BB) domain, a deleted carboxy transferase (CT) domain and having a functional biotin carboxylase (BC) domain that binds soraphen or a peptide consisting essentially of a functional ACCase biotin carboxylase domain. The Action further alleges that the specification does not provide any partial structure of such a peptide having a deleted BB domain, a deleted CT domain and having a functional BC domain that binds soraphen or any physical, chemical characteristics or functional characteristics coupled with a known or disclosed correlation between structure and function. The Action additionally states that the specification discloses a single peptide, SEQ ID NO:2, wherein said functional biotin carboxylase domain binds to soraphen, but alleges that this does not provide a description of a peptide comprising an ACCase having a deleted BB domain, a deleted CT domain and having a functional BC domain that binds soraphen or a peptide consisting essentially of a functional ACCase BC domain that would satisfy the standard set out in *Enzo Biochem, Inc. v. Gen-Probe, Inc.* (296 F.3d 1316, 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002))

As an initial matter and as discussed in Applicants' two previous responses, the disclosure in the specification of an embodiment comprising a construct that only contains the BC domain of ACCase does not limit the invention to this embodiment. Thus, the meaning of "deleted" includes an ACCase containing more of the sequence than the BC domain, but the other domains are rendered non-functional using common molecular biology techniques.

The BC domain found in the claims is not merely a BC domain—it is the BC domain of an ACCase. Furthermore, it is not the mere presence of the BC domain that is claimed. The BC domain as claimed has been manipulated by molecular biology techniques routine in the art at the time the invention was filed such that the end result is a peptide comprising an ACCase

having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen. Applicants define "functional" with respect to the BC domain of ACCase as binding to soraphen, as pointed out in Applicants' previous two responses.

Furthermore and contrary to the assertion in the Action, Applicants provide multiple examples in the specification of peptides comprising BC domains of ACCase retaining functionality (i.e., a soraphen binding site) and having a deleted biotin binding domain and a deleted carboxy transferase domain which are normally found in naturally-occurring ACCase. These are presented structurally as SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, or 16 and are representative examples of ACCase peptides having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen as claimed herein.

Applicants additionally point out that AcetylCoA carboxylases (from a wide variety of organisms) and their structures were well known in the art at the time the present application was filed (*See*, for example, Roessler et al., *Ann. N. Y. Acad. Sci.* 721: 250-256 (1994); Elborough et al., *Biochem. J.*, 301:599-605 (1994); Roesler et al., *Plant Physiol.* 105: 611-617 (1994); Podkowinski et al., *Proc. Natl. Acad. Sci.* 93: 1870-1874 (1996); Gornicki et al., *Proc. Natl. Acad. Sci.* 94: 14179-14184 (1997); U.S. Patent No. 6,455,688; and U.S. Patent No. 6,514,726) (copies of the non-patent references are enclosed herewith). These references illustrate that ACCases and the structure and function of their BB, BC and CT domains were well known at the time of the filing of the present application, and further, that ACCases from a wide variety of organisms were understood to share significant homology (*See*, for example, Roessler et al., page 253; Elborough et al., page 602;. Gornicki et al., page 14181; and Podkowinski et al., page 1873).

The Guidelines for Examination of Patent Applications state that what is well known in the art need not be described in detail in the specification (Guidelines for Examination of Patent Applications Under the 35 U.S.C.112 ¶ 1, Written Description Requirement, Federal Register vol. 66, page 1105, column 3). Thus, based on the present disclosure and what was known in the art about the structure of ACCase polypeptides, one of skill would clearly understand what was encompassed by a peptide comprising an AcetylCoA carboxylase having a deleted biotin binding domain, having a deleted carboxy transferase domain and having a functional biotin carboxylase

domain that binds soraphen or a peptide consisting essentially of a functional ACCase biotin carboxylase domain as claimed by the present invention. Therefore, applicants respectfully submit that the presently claimed invention meets the standards set out in both Enzo and Lilly.

Finally, applicants point out that a description in a claim of a lack of function or a deletion of a domain or portion of a domain such that it lacks function provides sufficient description such that one of skill in the art would understand the scope of what is claimed. As pointed out in applicants' previous response, the specific use of the term "deleted" to describe and claim an invention is common in patent claims, and several examples were provided of such use (*See*, U.S. Patent No. 6,911,205; U.S. Patent No. 6,962,708; and U.S. Patent No. 7,022,816).

Furthermore, the U.S. Court of Appeals for the Federal Circuit (CAFC) confirmed in *Invitrogen Corp. v. Clontech Laboratories, Inc.,* (429 F.3d 1052, 77 U.S.P.Q.2d 1161 (Fed. Cir. 2005)) that such a claim can satisfy the written description requirement. In *Invitrogen,* the applicants claimed an isolated DNA molecule comprising a nucleotide sequence encoding a polypeptide having DNA polymerase activity and substantially no RNaseH activity, wherein said nucleotide sequence is derived from a Moloney murine leukemia virus (M-MLV) nucleotide sequence. *Id.* at 1074. The dependent claims recited "no detectable RNAse H activity" and "lacks RNAse activity." *Id.* The Invitrogen disclosure provided a representative embodiment as well as test data showing that the enzyme produced by the listed sequence had the claimed features of DNA polymerase activity without RNAse H activity. *Id.* at 1076-1077. The District Court and the CAFC found that such a recitation of "no detectable" or "lacks" satisfied the written description requirement of § 112. *Id.* at 1074 , 1079. Similarly, based on the representative structures and the description provided in the specification of the present invention, as well as the information about ACCases generally known in the art, one of skill in the art would know what was encompassed by a peptide comprising an AcetylCoA carboxylase having a deleted biotin binding domain, having a deleted carboxy transferase domain and having a functional biotin carboxylase domain that binds soraphen or a peptide consisting essentially of a functional ACCase biotin carboxylase domain as claimed by the present invention. Accordingly, the specification of presently claimed invention satisfies the written description requirement.

For the forgoing reasons it is submitted that the rejection under 35 USC 112, first paragraph, should be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

A. Bailey et al.

The Action states that claims 1-3, 10, 12 and 23-25 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Bailey et al. (*Mol. Gen. Genet.* 249: 191-201 (1995)). Action, page 5. The Action states that applicants' previous arguments were non-persuasive because the claims do not set forth any structural details of a peptide that binds to soraphen. *Id.* The Action further states that in the absence of structural details the art reads on the claimed invention. *Id.*

As discussed above, applicants respectfully submit that the application provides representative examples of a peptide comprising an ACCase having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen as claimed herein or a peptide consisting essentially of a functional ACCase biotin carboxylase domain as claimed by the present invention in SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, or 16. Thus, the description provided in the specification of the present invention, including the representative examples, in combination with what was known in the art at the time the present application was filed, provide sufficient structural information regarding the peptides of the present invention.

Furthermore, applicants point out that a rejection under 35 U.S.C. § 102(b) requires that every element of the claimed invention be present in the cited reference. As applicants have clearly shown in their previous response that Bailey et al. fails to teach or suggest every element of the presently claimed invention since Bailey et al. does not teach or suggest a peptide comprising an Acetyl CoA carboxylase (ACCase) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen. As the previous Action conceded, Bailey et al. does not teach that the deduced peptide of Bailey et al. binds to soraphen or has a soraphen dissociation constant from 10^{-7} to 10^{-14}. Contrary to the assertion in the Action that simply because the deduced peptide discussed in Bailey et al. is from a gene isolated from the same source it must necessarily read on claim 10 and 12, Shen et al. (provided with the response dated January 11, 2007) clearly shows that the BC domain discussed in Bailey et al. does not inherently disclose a BC domain that binds to soraphen or has a soraphen dissociation constant from 10^{-7} to 10^{-14}.

Furthermore, since the focus of Bailey et al. was to determine which amplified fragment would be predicted to be that of an ACCase, and thus could be used to obtain the full sequence of the ACCase in *U. maydis*, the reference never discusses a peptide having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen.

As is known in the art, eukaryotic ACCases have two catalytically active domains: the BC domain and the CT domain. Further, applicants note that because the CT active site is a classic deep, hydrophobic cleft, one would expect that screens for small molecule modulators of ACCase activity using full-length enzyme would primarily turn up CT inhibitors and this appears to be the case. The inventors of the present invention believe that to the best of their knowledge, with the exception of soraphen (which was not identified using a target based approach), all specific and high affinity ACCase inhibitors identified to date target the CT domain.

The focus of the present invention is the development of a process by which novel small molecule modulators of ACCase activity that bind to and act at the soraphen binding site can be identified. At the time the present invention was made, there were no published reports of recombinant expression of native ACCase or sub-domains thereof. It is important to note that identification of a domain by analyzing a protein sequence does not guarantee that one will be able to express that domain in a native form when it is isolated from the rest of the polypeptide. The present inventors, by expressing an isolated native BC domain, have demonstrated that the isolated domain indeed binds soraphen with the same affinity as that of the full-length enzyme and therefore could be used to identify soraphen-like inhibitors of ACCase and they have shown this with isolated BC domains from different organisms.

Additionally, the inventors surprisingly discovered that the recombinant BC domains of the present invention are much more stable and can be expressed at much higher levels than the full-length enzyme. It is important to note that while ACCase has been one of the most studied enzymes in biochemistry, the first published report of recombinant expression and purification of a biologically active eukaryotic ACCase was not until 2003 (Weatherly et al., Biochem. J. 380: 105-110 (2004)). The high stability and high level of expression in the recombinant BC domains discovered by the present inventors has allowed the development of a fluorescence polarization soraphen competition binding assay for high through-put screening to specifically identify small molecules that bind to and act at the soraphen binding site. Identification of such inhibitors

using full-length enzyme in an activity assay would be significantly more difficult since primarily BC and CT active site inhibitors would be pulled out.

Accordingly, applicants respectfully submit that claims 1-3, 10 and 12 are novel over Bailey et al., and thus, respectfully request that this rejection be withdrawn.

B. Schulte et al.

The Action states that claims 1-2, 10 and 12 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Schulte et al. (*Proc. Natl. Acad. Sci.* 94: 3465-3470 (1997)). Action, page 4. Specifically, the Action refers to the dendrogram in Figure 5 as disclosing deduced amino acid sequences covering the BC domain of yeast ACCase. Action, page 5. The Action states that the although the reference does not teach that the peptide binds to soraphen or has a soraphen dissociation constant of from 10^{-7} to 10^{-14}, given that the peptide is isolated from the same source as the instantly claimed peptide, the disclosed prior art reads on claims 10 and 12.

Similar to the discussion above concerning Bailey et al., Shulte et al. fails to disclose every element of the present invention. Specifically, Shulte et al. fails to teach or suggest a BC domain of any organism, including yeast, in which the BC domain binds to soraphen or has a soraphen dissociation constant of from 10^{-7} to 10^{-14}. Further, Shulte et al. fails to teach or suggest a peptide having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase domain, wherein said peptide binds to soraphen.

Shulte et al. provides no discussion of what portion of the BC domain is represented in the dendogram and as seen with the Bailey et al. reference, simply referring to a portion of a gene as a BC domain does not inherently disclose a BC domain that binds to soraphen. Furthermore, as discussed above, the identification of a domain by analyzing a protein sequence does not guarantee that one will be able to express that domain in a native form when it is isolated from the rest of the polypeptide. Thus, unless the peptides of these references specifically state that they are capable of binding soraphen, it cannot be taken that such would be inherent based on a deduced sequence.

Finally, since the Action specifically cites to the BC domain of the yeast ACCase of Figure 5 of Shulte et al., it is relevant to discuss information about that disclosure provided by the original source of that particular disclosure, which is Al-Feel et al. (*Proc. Natl. Acad. Sci.* 89:

4534-4538 (1992); cited as reference number 50 in Shulte et al.) This is particularly true since Shulte et al. provides nothing more in the dendrogram than names of the comparative organisms.

As applicants previously discussed, the Al-Feel et al. reference discusses the cloning of the yeast *FAS3* gene. In Al-Feel et al., the nucleotide sequence of the entire gene was reported, and the *putative* BC domain within the gene was determined, based solely on *deduced* amino acid sequence comparison with ACCase from rat and chicken (page 4534, first column, third paragraph). Importantly, Al-Feel et al. also reported the gene having a putative biotin binding ("Biotin Binding Site") and a carboxytransferase ("Transcarboxylase") domain. Therefore, neither Shulte et al. or Al-Feel teach or suggest an ACCase having a deleted biotin binding domain, having a deleted carboxytransferase domain or having a functional biotin carboxylase domain that binds to soraphen or has a soraphen dissociation constant of from 10^{-7} to 10^{-14}. As applicants pointed out in their previous response, Schulte et al. merely studied the 5' portion of the ACCase coding region because the clones that they had isolated from rapeseed differed in that portion of the putative transcripts.

Accordingly, applicants respectfully submit that Schulte et al. fails to teach each of the recitations of the claimed invention as required under 35 U.S.C. 102(b) and thus, respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

The Action states that claims 1-3, 10, 12 and 13 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Bailey et al. or Schulte et al. in view of Trubetskoy et al., U.S. Pat. 7,098,032. As discussed above, neither Bailey et al. nor Schulte et al., alone or in any combination, teach or suggest each of the recitations of the claimed invention. Trubetskoy et al. fails to remedy the deficiencies of Bailey et al. or Schulte et al. Therefore, a combination of references containing either or both Bailey et al. and Schulte et al. with Trubetskoy et al., which was only used by the Examiner to allege a teaching of the pH range found in claim 13 of the present invention, cannot support a rejection under § 103(a). Accordingly, Applicants respectfully request that this rejection be withdrawn.

Conclusion

In view of the remarks presented herein, Applicants respectfully submit that this application is in condition for allowance, which action is respectfully requested.

The Commissioner is authorized to charge Deposit Account No. 50-0220 in the amount of $120.00 as the fee for a one-month extension of time. This amount is believed to be correct. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

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Enclosures:

Roessler et al., *Ann. N. Y. Acad. Sci.* 721: 250-256 (1994);
Elborough et al., *Biochem. J.,* 301:599-605 (1994);
Roesler et al., *Plant Physiol.* 105: 611-617 (1994);
Podkowinski et al., *Proc. Natl. Acad. Sci.* 93: 1870-1874 (1996);
Gornicki et al., *Proc. Natl. Acad. Sci.* 94: 14179-14184 (1997)